Regulation of mouse mast cell surface FcεRI expression by dexamethasone

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Abstract

It is now clear that the mast cell's functional response to IgE-dependent stimulation can be influenced significantly by the level of expression of the high-affinity IgE receptor (FcεRI) on the cell's surface. Thus, modulation of FcεRI surface expression represents a potentially important mechanism for regulating mast cell activity in allergic reactions. In this study, we examined whether a glucocorticoid, dexamethasone (DEX), can influence levels of mast cell FcεRI expression either in the presence or absence of IgE, an up-regulator of the mast cell surface FcεRI level. In the absence of IgE, DEX decreased the surface FcεRI levels in mouse peritoneal mast cells, mouse bone marrow-derived cultured mast cells and a mouse mast cell line, CLMC/C57.1. Moreover, DEX also partially suppressed the ability of IgE to enhance surface expression of FcεRI in these cells. Three different glucocorticoids, DEX, methylprednisolone and hydrocortisone, suppressed FcεRI expression in mast cells, whereas sex steroids, i.e. estradiol, progesterone and testosterone, did not, indicating that the FcεRI-suppressing effect is glucocorticoid specific. On the other hand, DEX did not affect levels of FcεRI α, β or γ mRNA, suggesting that its ability to decrease surface FcεRI reflects a post-transcriptional mechanism. Finally, DEX-treated mast cells showed a reduced degranulation response to antigenic stimulation through down-regulation of surface FcεRI expression in addition to DEX-induced changes in downstream signals. These results show that mast cell surface FcεRI expression is suppressed by glucocorticoids in both the presence and absence of IgE, and suggest that reduction of mast cell surface FcεRI levels may be one of the favorable anti-allergic actions of glucocorticoids.

Introduction

IgE-mediated stimulation of mast cells and basophils is an important initial event in type I allergic reactions. The high-affinity receptor for IgE (FcεRI) is abundantly expressed on these cells and following stimulation via FcεRI, mast cells and basophils release bioactive chemical mediators such as histamine, resulting in the initiation of allergic reactions (1,2). FcεRI is required for mast cells to initiate IgE-mediated allergic reactions, because mice deficient in FcεRIα fail to exhibit allergic reactions even in the presence of antigen and antigen-specific IgE (3,4). Several lines of evidence have shown that levels of FcεRI on the surface of mast cells and basophils can be regulated by extracellular factors (5–10). For example, we (6,7,11,12) and others (10,13) have already reported that IgE can potently enhance mast cell surface FcεRI expression, and the up-regulation of surface FcεRI levels is functionally important because mast cells with a high level of FcεRI on their surface show enhanced sensitivity and a stronger response to antigenic stimulation. In accord with advances in our understanding of the mechanisms which can up-regulate mast cell and basophil
surface FcεRI levels in vitro and in vivo, increasing consideration is being given to therapeutic approaches that can influence levels of expression of FcεRI. Recombinant humanized anti-IgE antibody (E25) was recently reported to have benefit in patients with allergic asthma (14, 15). In parallel with a striking reduction in free IgE (<5% of initial levels), which includes IgE recognizing allergen-specific epitopes (14, 15). Administration of E25 also resulted in both reduced expression of basophil FcεRI expression and diminished skin sensitivity to allergen challenge (9). Because E25 antibody does not react with FcεRI-bound IgE on the surface of mast cells and basophils, the decrease in cell surface FcεRI levels probably does not reflect any direct action of E25 on FcεRI+ cells, but indirect consequences of the decreased concentrations of serum IgE (9, 16).

Although surface FcεRI expression and FcεRI-mediated cellular function may be regulated by complex mechanisms, it is reasonable to expect that manipulations which diminish surface levels of FcεRI on mast cells may also decrease the intensity of antigen- and IgE-mediated allergic reactions. In the 1980s, Benhamou et al. (17) and Robin et al. (18) separately reported that a corticosteroid, dexamethasone (DEX), can exhibit suppressing effects on mouse mast cell FcεRI expression in vitro. However, at that time the ability of IgE to induce the dramatic up-regulation of mast cell FcεRI expression was not known, so the effects of glucocorticoid treatment on this process were not investigated. In this study, we analyzed the action of DEX on mast cell surface FcεRI levels and demonstrate that DEX can suppress mast cell FcεRI levels either in the presence or absence of IgE. Some of these results have been reported in abstract form (19).

Methods

Steroids

DEX, hydrocortisone, methylprednisolone, progesterone, estradiol and testosterone were purchased from Wako Pure Chemical Industries (Osaka, Japan), and dissolved in ethanol at a stock concentration of 20 mM.

Cell culture

Peritoneal cells from BALB/c mice were cultured in DMEM (Gibco/BRL, Gaithersburg, MD) supplemented with 10% FCS (Gibco), 2 mM L-glutamine (Gibco), recombinant mouse stem cell factor (SCF) at 50 ng/ml (PeproTech, London, UK), 50 µM 2-mercaptoethanol and antibiotics (penicillin/streptomycin) (Gibco). Mast cells comprised ~3-5% of the total peritoneal cells as assessed by May–Grünwald–Giemsa stain. Before analysis of changes in the mast cell surface FcεRI level, cells were cultured for indicated times with or without a steroid and/or mouse ascites IgE (5 µg/ml).

Bone marrow-derived cultured mast cells (BMCMC), >99% purity, were generated by culturing femoral bone marrow cells of BALB/c mice (SLC, Shizuoka, Japan) in 20% WEHI-3 cell supernatant-conditioned DMEM supplemented with 10% FCS, L-glutamine, 2-mercaptoethanol and antibiotics for 5–6 weeks.

Cloned mast cells, Cl. MC/C57.1 (C57) cells, originally derived from a BALB/c mouse (20, 21) were maintained in DMEM supplemented with 10% FCS, L-glutamine and 2-mercaptoethanol.

Flow cytometric analysis

Flow cytometric analysis of mast cells was performed essentially as reported previously (6, 7). In brief, mouse peritoneal mast cell preparations were preincubated for 15 min with 2,4G2 mAb (PharMingen, San Diego, CA) at 10 µg/ml to block the low-affinity binding of IgE to FcγRII/III. Cells were then incubated at 4°C with mouse monoclonal IgE (SPE-7, Sigma, St Louis, MO) at 10 µg/ml for 50 min and then for the last 25 min with a biotinylated rat anti-mouse c-kit antibody (PharMingen) at 15 µg/ml. After washing, the cells were stained with FITC–rat anti-mouse IgE antibody (PharMingen) at 10 µg/ml and phycoerythrin (PE)–streptavidin (Sigma) at 14 µg/ml for 30 min. Stained cells were analyzed using an Epics XL System II (Coulter, Miami, FL). At least 20,000 peritoneal cells in each sample were analyzed and >500 mast cells (IgE+ c-kit+) were assessed. An instrument setting for the flow cytometer that was appropriate for analysis of peritoneal cells was determined in preliminary experiments and was not changed throughout this study. The median values of fluorescence intensity of stained mast cells were converted to molecules of equivalent soluble fluorochrome (MESF) units by using Quantum 25 microbead standards (Flow Cytometry Standards, San Juan, Puerto Rico).

For flow cytometry of mouse BMCMC or C57 cells, cells were preincubated with 2,4G2 mAb and then incubated with IgE, followed by staining with FITC–anti-IgE antibody. At least 10,000 mast cells were studied to assess their surface FcεRI expression.

Before analyzing surface FcγRII/III, mouse BMCMC were incubated on ice for 1 h with 2,4G2 mAb and then stained with PE–goat anti-rat IgG (Caltag, Burlingame, CA) at 5 µg/ml for 30 min.

Northern blot hybridization

Following culture of C57 cells with or without IgE at 5 µg/ml and/or DEX at 100 nM, the cells were harvested, and the total RNA was extracted using RNA STAT-60 (Tel-Test, Friendswood, TX) according to the manufacturer’s instructions. Total RNA (10 µg/each lane) was applied to formaldehyde–agarose gel and transferred to a nylon membrane (Biodyne B; Pall BioSupport, East Hills, NY).

Mouse FcεRI α, β and γ chain cDNAs were obtained as reported previously (22, 23). Plasmids containing their cDNA were amplified in Escherichia coli and then extracted using a Maxiprep isolation kit followed by enzyme digestion. 32P-labeled probes were produced using a Rediprime II DNA labeling system (Amersham Pharmacia Biotech, Tokyo, Japan).

Northern blot hybridization was done in a QuikHyb Hybridization Solution (Toyobo, Tokyo, Japan) overnight at 65°C and blots were washed under stringent conditions. The hybridized blots were then exposed to an imaging plate (BAS SR; Fuji Photo Film, Tokyo, Japan), and radioactive bands were visualized and measured using Fojix Bas 2500 (Fuji Photo Film).
Fig. 1. Dose-dependent effect of DEX on surface FcεRI expression in mouse peritoneal mast cells. Peritoneal cells from six BALB/c mice were combined and then cultured for 48 h with recombinant mouse SCF at 50 ng/ml, and with or without IgE (at 5 µg/ml) and various concentrations of DEX. Surface FcεRI expression on mast cells was analyzed by flow cytometry and presented in MESF units (see Methods). Data are indicated as the mean ± SEM (n = 3). *P < 0.05, ***P < 0.0001 versus corresponding values for cells cultured without DEX.

Activation of mast cells

C57 cells were cultured for 20 h with or without mouse ascites IgE at 5 µg/ml and/or DEX at 100 nM. The cells were then incubated with IgE at 5 µg/ml for 2 h on ice to fully saturate their surface FcεRI, washed with PIPES buffer containing 0.1% BSA, and then resuspended in PIPES buffer containing 1 mM Ca²⁺ and 0.4 mM Mg²⁺. The cells were stimulated with either DNP-HSA (Sigma) or ionophore A23187 (Sigma) for 45 min at 37°C and histamine released into the supernatant was measured using an automated fluorimeter as described by Siraganian (24). The percentage of histamine release was calculated by the following formula: 100×(released histamine – spontaneous release)/(total histamine – spontaneous release). Spontaneous histamine release did not exceed 7% of the total histamine content.

Statistics

Unless otherwise specified, all data were expressed as the mean ± SEM and all differences between values were compared by the two-tailed Student’s t-test (unpaired).

Results

DEX can suppress levels of mast cell surface FcεRI expression

We analyzed the effect of DEX on FcεRI expression using mast cells cultured in both the absence and presence of IgE. As shown in Figs 1 and 2, DEX suppressed the level of surface FcεRI expression on mouse peritoneal mast cells (Fig. 1) and BMCMC (Fig. 2) in a dose-dependent fashion. For both types of mast cells, statistically significant inhibition was observed when DEX at 10 or 100 nM was included in the culture medium (Figs 1 and 2A). Importantly, suppression of the surface FcεRI level by DEX was observed in peritoneal mast cells and BMCMC even in the presence of IgE, indicating that incubation with IgE does not abolish the down-regulating effect of DEX on mast cell FcεRI levels. The effect of DEX was time dependent: an apparent decrease in the FcεRI level was observed after as short as 6 h of culture of BMCMC, in either the presence or absence of IgE (Fig. 2B).

In order to examine whether DEX can actively suppress levels of IgE-bound FcεRI, BMCMC were cultured with IgE at 5 µg/ml for 4-day, which is a sufficient period for full induction of surface FcεRI, before treatment of the cells with DEX. As shown in Fig. 3, the maximal level of surface FcεRI expression on BMCMC, obtained after 4-day culture with IgE at 5 µg/ml, was significantly reduced by the treatment with DEX for 20 h, indicating that DEX treatment can enhance the disappearance of IgE-bound FcεRI from the cell surface.

It should be noted that the effects of DEX on levels of mast cell FcεRI did not result from apoptosis of the mast cells. As detected by TUNEL staining followed by flow cytometric analysis (25), we observed no increase in apoptotic BMCMC or C57 cells treated with DEX at 100 nM for up to 24 h (data not shown). Furthermore, the effect of DEX on mast cell FcεRI expression did not appear to reflect a general suppressive effect on Fc receptor expression, because treatment of BMCMC with DEX at 100 nM, which decreased the level of FcεRI (Fig. 4A), had no effect on surface expression of FcyRII/III (Fig. 4B).

Glucocorticoids, but not sex steroids, can reduce mast cell surface FcεRI expression

In the next series of experiments, we investigated the effects of various steroids on mast cell surface FcεRI levels. The mouse mast cell line, C57 cells, were cultured with or without IgE (at 5 µg/ml) and/or one of various steroids (at 100 nM) for 16 h, and their FcεRI expression was analyzed by flow cytometry. As shown in Fig. 5(A), glucocorticoids, including DEX, hydrocortisone and methylprednisolone, reduced mast cell FcεRI expression, while sex steroids, i.e. estradiol, progesterone and testosterone, failed to affect the surface level of FcεRI. Importantly, the level of surface FcεRI expression was also partially suppressed by the glucocorticoids, but not by the sex steroids (Fig. 5B), when we tested mast cells that were undergoing increases in levels of FcεRI in the presence of IgE (at 5 µg/ml).

Analysis of FcεRI α, β and γ mRNA levels in mast cells cultured with DEX

To examine whether DEX might influence FcεRI expression at the transcriptional level, we assessed the mRNA levels of each subunit of FcεRI by Northern blot hybridization. However, we observed no obvious differences in the mRNA levels for the FcεRI α, β and γ chains in C57 cells cultured with or without IgE (at 5 µg/ml) and/or DEX (at 100 nM), even though a DEX-induced decrease in the surface FcεRI level was clearly detected by flow cytometric analysis (Fig. 6). Because treatment with DEX resulted in a modest decrease (by ~40%) in mRNA levels of β-actin without affecting RNA recovery from
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Fig. 2. (A) Dose- and (B) time-dependent effects of DEX on surface FcεRI expression by mouse BMCMC. (A) BMCMC obtained from BALB/c mice were cultured for 16 h with or without ascites IgE (at 5 μg/ml) and/or various concentrations of DEX. (B) BMCMC were cultured with or without IgE (at 5 μg/ml), in addition to either DEX at 100 nM or vehicle alone (ethanol 0.0005%) for 6, 16 or 26 h. Data are the mean ± SEM (n = 3). **P < 0.001, ***P < 0.0001 versus corresponding values for cells cultured without DEX.

Fig. 3. Effect of DEX on BMCMC with maximal levels of surface FcεRI expression. BALB/c mouse BMCMC were cultured with or without IgE at 5 μg/ml for 5 day and for the last 20 h with either DEX at 100 nM or vehicle (ethanol at 0.0005%). Surface FcεRI expression was analyzed by flow cytometry. Data are indicated as the mean ± SEM (n = 3). **P < 0.001 versus corresponding values of cells cultured without DEX.

C57 cells, thus normalized ratios (FcεRI each chain mRNA:β-actin mRNA) were accordingly elevated by ~50%. However, relatively constant ratios of FcεRI α chain:γ chain (0.8–1.0 for DEX-untreated cells versus 0.9–1.2 for DEX-treated cells, compared with the corresponding ratio of 0 h sample in Fig. 6)

Fig. 4. Surface expression of (A) FcεRI and (B) FcγRI/III on mouse BMCMC cultured with or without DEX. BALB/c mouse BMCMC were cultured for 20 h with or without IgE at 5 μg/ml, in addition to either DEX at 100 nM or vehicle (ethanol at 0.0005%). Cells were stained for either surface FcεRI or FcγRI/III expression, as described in Methods.
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Fig. 5. Effects of various steroids on surface FcεRI expression in a mouse mast cell line. Cl.MC/C57.1 (C57) mouse mast cells were cultured for 16 h without (A) or with (B) IgE at 5 µg/ml, in addition to either steroid (at 100 nM) or vehicle (ethanol at 0.0005%). MP, methylprednisolone; HC, hydrocortisone; PROG, progesterone; EST, estradiol; TESTO, testosterone. Data are the mean ± SEM (n = 3). **P < 0.001 versus values of cells cultured with vehicle alone, indicated as ‘None’.

Fig. 6. Levels of (A) surface FcεRI expression, and (B) FcεRI α, β and γ chain mRNA in C57 mast cells treated with DEX. C57 mast cells were cultured for 4 or 12 h with or without IgE at 5 µg/ml and either DEX (at 100 nM) or vehicle (ethanol at 0.0005%). At each time point, cells were harvested, and their surface FcεRI and FcεRI mRNA expression were analyzed by flow cytometry and Northern blot hybridization respectively. Densities of mRNA bands for FcεRI α, β and γ chains were measured by densitometry, but none of the α, β or γ chain mRNAs showed an apparent difference between DEX-treated and -untreated cells. Two other experiments using C57 cells gave similar results.

or β chain; γ chain (0.8–1.0 for DEX-untreated cells versus 0.7–1.0 for DEX-treated cells) further suggest that DEX does not influence mRNA levels of any of the FcεRI α, β or γ chains.

We also performed RT-PCR analysis of BMCMC cultured with or without IgE and/or DEX, but again, no apparent differences in the density of amplified bands for the FcεRI α, β and γ chains were found (data not shown). These results suggest that the effects of DEX on mast cell surface FcεRI levels were mediated by post-transcriptional regulation.

**DEX-treated mast cells with suppressed FcεRI levels exhibit diminished IgE-dependent activation**

To assess whether the DEX-induced changes in mast cell FcεRI levels are associated with a functional change, we cultured C57 cells for 20 h with or without IgE and/or DEX, and then stimulated the cells with specific antigen or a non-specific secretagogue (calcium ionophore A23187). In accord with our previous reports (6,7,11) mast cells with increased level of surface FcεRI expression after culture with IgE demonstrated an enhanced histamine release reaction to FcεRI-dependent stimulation, although the percentage of release caused by non-specific stimulation with ionophore A23187 was virtually unchanged (Fig. 7). In contrast, mast cells with decreased levels of FcεRI expression due to exposure to DEX demonstrated reduced histamine release, whether or not the cells had also been cultured for 20 h in the presence of IgE (Fig. 7). Compared with mast cells that had not been treated with DEX, DEX-treated cells showed suppressed histamine release on stimulation with a given concentration of antigen, in addition to decreased sensitivity to antigen stimulation; however, the percentage of histamine release caused by stimulation with A23187 was not changed by treatment of cells with DEX (Fig. 7).

Although DEX-treated mast cells showed suppressed histamine release compared with untreated mast cells, the effect of DEX may be due to the changes in either (or probably both) surface FcεRI levels and/or intracellular signal transduction. In the last series of experiments, we examined whether the DEX-induced decrease in surface FcεRI levels (by 30–50%) is functionally significant. Following treatment for 20 h with or without DEX at 100 nM but without IgE, C57 mast cells were sensitized with IgE at 5 µg/ml on ice for various time periods,
Discussion

Glucocorticoids are recognized as very effective medications for various allergic diseases, including bronchial asthma, and it is widely accepted that allergic inflammation is potently suppressed by these agents. Glucocorticoids act not only on lymphocytes, but also on eosinophils (26), basophils (27–29) and other types of inflammatory cells, and can suppress the cells’ effector functions, such as the release of chemical mediators, thus reducing the severity of allergic inflammation at the sites of allergic diseases.

Several effects of glucocorticoids on mast cells have also been reported (17,18,30–32) including reduction in the numbers of tissue mast cells (33), and suppression of IgE- and antigen-induced responses such as leukotriene release (18) and cytokine production (31). In spite of these other anti-allergic actions of glucocorticoids, glucocorticoid-induced modulation of mast cell FcεRI expression may be of particular importance because such effects theoretically can influence all FcεRI-mediated downstream events.

In this study, we have demonstrated that DEX not only can suppress the baseline levels of unoccupied FcεRI on mast cells, but also can result in reduction of the FcεRI levels in cells that have FcεRI occupied by IgE and have undergone IgE-dependent up-regulation of FcεRI expression. Although the regulation of mast cell surface FcεRI expression is not fully understood, studies using a mast cell line, i.e. rat basophilic leukemia (RBL) cells, showed that an important site of IgE-mediated FcεRI up-regulation is at the surface of the cells: IgE stabilizes FcεRI and reduces the loss of receptors from the cells’ surface (4,34,35). DEX may also influence this process, because a significant portion of FcεRI on mast cells was lost from the surface during treatment with DEX. However, it should be noted that the precise cellular component(s) that are targets of DEX action may be different from those affected by IgE because DEX induces reductions in both IgE-occupied and -unoccupied FcεRI from the surface, whereas IgE of course stabilizes only IgE-occupied FcεRI (4). Recently, there has been considerable progress in research on the intracellular mechanisms of corticosteroid action: corticosteroids, coupled with their receptors, suppress the transcription of various inflammatory molecules, whereas they enhance the transcription of other molecules possessing mainly anti-inflammatory activities (36,37). However, the exact mechanism(s) responsible for the ability of DEX to down-regulate levels of surface FcεRI remain(s) to be determined.

The level of mast cell surface FcεRI expression clearly can influence the cell’s functional response to FcεRI-dependent stimulation (6,7,11,12); we found that this is also true in DEX-treated mast cells. Thus, the decrease in surface FcεRI level on C577 cells induced by treatment of the cells with DEX was accompanied by a significantly reduced degranulation response to antigenic stimulation. Although the consequences of DEX action on mast cells may vary among different species and for the different biological functions of mast cells, the release of leukotrienes and proinflammatory cytokines from rodent mast cells in vitro is potently suppressed by corticosteroids (18,31). Previous work has suggested that the magnitude of corticosteroid effects on mast cell degranulation may vary among mast cells of different phenotypes and even among different batches of mast cells of a single phenotype (30). However, our results consistently showed that pretreatment of C577 cells with DEX at 100 nM for 20 h significantly reduced the histamine release response to antigen challenge, but not to non-IgE-mediated stimulation with calcium ionophore. Our findings are in line with the results reported by Robin et al. (18) and Benhamou et al. (17), who showed that BMCMC treated for 24 h with DEX but without IgE...
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Fig. 8. Functional analysis of DEX-treated and -untreated mast cells with various levels of surface-bound IgE. C57 mouse mast cells were cultured for 20 h with either DEX (at 100 nM) or vehicle (ethanol at 0.0005%) and then sensitized with IgE at 5 µg/ml for either 5, 20, 60 or 120 min on ice to allow various levels of surface IgE binding (A–C). Surface IgE levels of DEX-untreated (A) and -treated (B) cells expressed in MESF units are indicated (C). The cells were washed and then stimulated with antigen (DNP-HSA at 0.1 or 1 ng/ml) and percent histamine release was measured (D). Data are indicated as the mean ± SEM (n = 3). *P < 0.05, **P < 0.001, ***P < 0.0001 versus percent release for cells cultured without DEX and then sensitized with IgE for 120 min. *P < 0.05, **P < 0.001, ***P < 0.0001 versus corresponding values for cells cultured without DEX and sensitized with IgE for the same time period. Two other experiments showed similar results.

demonstrated decrease in both surface FcεRI levels and β-hexosaminidase release to IgE-dependent stimulation. In addition, we have found that the DEX-induced decrease in both surface FcεRI levels and IgE-mediated degranulation can also occur in IgE-containing situations. In both the absence and presence of IgE during culture, the effect of DEX on mast cell degranulation was even more pronounced when the mast cells were stimulated with a low concentration of antigen, since DEX reduced not only the intensity of histamine release response, but also the sensitivity of the cells to antigen challenge. However, it could be reasonably noted that DEX-induced functional modification in mast cells is additionally mediated by other, intracellular mechanisms (17,30) since DEX-treated mast cells showed a more profound decrease in degranulation than DEX-untreated mast cells with almost similar levels of surface-bound IgE (see Fig. 8).

Recent results in clinical trials on anti-IgE therapy have suggested that effects of the treatment on levels of cell surface FcεRI expression are one important point to be considered when devising therapeutic strategies for IgE-mediated allergic diseases. Anti-human IgE therapy is known to potently suppress the serum IgE concentration, resulting in reduced basophil surface FcεRI levels (9,14). This antibody demonstrates not only clinical benefit in patients with allergic asthma (15) but also a suppressive effect on the skin test, indicating the response of cutaneous mast cells to antigen is reduced (9). The findings presented herein provide further support for the notion that levels of mast cell surface FcεRI expression may be one of the important therapeutic targets in treating allergic diseases. Although the precise molecular mechanisms whereby glucocorticoids decrease surface expression of FcεRI on mast cells remain to be determined, their suppressive effects on surface expression of FcεRI, whether or not it is occupied with IgE, may represent one of the clinically important anti-allergic actions of glucocorticoids.
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Abbreviations

BMMC: bone marrow-derived cultured mast cells
C57 cells: C57 mouse mast cell line cells
DEX: dexamethasone
FceRI: high-affinity receptor for IgE
MESF: molecules of equivalent soluble fluorochromes
PE: phycoerythrin
RBL: rat basophilic leukemia
SCF: stem cell factor

References

1. Ishizaka, T. and Ishizaka, K. 1984. Activation of mast cells for mediator release through IgE receptors. Prog. Allergy 34:188.
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